

CLAIMS

WHAT IS CLAIMED IS:

- 5 1. An isolated nucleic acid encoding a fusion protein comprising:
- (1) the A subunit of Shiga-like bacterial toxin, or a truncated or mutated version thereof, said subunit having the nucleic acid sequence of SEQ ID NO:9, or a truncated or mutated
- 10 version thereof; and
- (2) human vascular endothelial growth factor, or a truncated or mutated version thereof, said growth factor having the nucleic acid sequence of SEQ ID NO:10, or a truncated or mutated version thereof;
- 15 wherein said fusion protein possesses ribosome inactivating activity.
2. The isolated nucleic acid of claim 1, wherein said fusion protein specifically binds to vascular endothelial growth factor
- 20 receptors.
3. The isolated nucleic acid of claim 2, wherein said fusion protein is capable of being internalized by a cell which expresses said receptors.

4. The isolated nucleic acid of claim 3, wherein said internalization occurs by endocytosis.

5 5. The isolated nucleic acid of claim 1, wherein said isolated nucleic acid has the nucleic acid sequence of SEQ ID NO:11.

6. An isolated polypeptide comprising:

(1) the A subunit of Shiga-like bacterial toxin, or a
10 truncated or mutated version thereof, wherein said subunit has the nucleic acid sequence of SEQ ID NO:9 or a truncated or mutated version thereof; and

(2) human vascular endothelial growth factor, or a truncated or mutated version thereof, wherein said growth factor
15 has the nucleic acid sequence of SEQ ID NO:10, or a truncated or mutated version thereof;

wherein said isolated polypeptide possesses ribosome inactivating activity.

20 7. The isolated polypeptide of claim 6, wherein said isolated polypeptide specifically binds vascular endothelial growth factor receptors.

8. The isolated polypeptide of claim 7, wherein said isolated polypeptide is internalized by a cell which expresses said receptors.

5 9. The isolated polypeptide of claim 6, wherein said internalization occurs by endocytosis.

10. The isolated polypeptide of claim 6, wherein said isolated polypeptide is encoded by the nucleic acid of SEQ ID NO:11.

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11. An expression vector, comprising:

(1) a nucleic acid encoding a fusion protein comprising the A subunit of Shiga-like bacterial toxin, or a truncated or mutated version thereof; and human vascular endothelial growth
15 factor, or a truncated or mutated version thereof; and

(2) a promoter sequence operably linked to said nucleic acid to allow expression of said nucleic acid;

said expression vector comprising the nucleic acid sequence of SEQ ID NO:11.

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12. The expression vector of claim 11, wherein said fusion protein is capable of specifically binding to vascular endothelial growth factor receptors.

13. The expression vector of claim 12, wherein said fusion protein is internalized by a cell which expresses said receptors.

5 14. A bacterial cell transformed with the expression vector of claim 11.

15. A method of inactivating ribosomes in a cell, comprising the steps of:

10 (a) contacting a cell with a polypeptide comprising:

(1) the A subunit of Shiga-like bacterial toxin, or a truncated or mutated version thereof, said subunit having the nucleic acid sequence of SEQ ID NO:9, or a truncated or mutated version thereof; and

15 (2) human vascular endothelial growth factor, or a truncated or mutated version thereof, said growth factor having the nucleic acid sequence of SEQ ID NO:10, or a truncated or mutated version thereof;

under conditions which permit said polypeptide to be
20 internalized into said cell and inactivate ribosomes in said cell.

16. The method of claim 15, wherein said fusion protein specifically binds vascular endothelial growth factor receptors.

17. The method of claim 16, wherein said fusion protein is internalized by a cell which expresses said receptors.

5 18. A composition for inhibiting endothelial cell growth in a patient, comprising:

(A) a fusion protein comprising the A subunit of Shiga-like bacterial toxin, or a truncated or mutated version thereof; and human vascular endothelial growth factor, or a truncated or mutated version thereof, said fusion protein possessing ribosome inactivating activity; and

(B) a pharmaceutically acceptable carrier;

wherein said A subunit of said Shiga-like bacterial toxin, or a truncated or mutated version thereof, is encoded by the nucleic acid sequence of SEQ ID NO:9, and wherein said human vascular endothelial growth factor, or a truncated or mutated version thereof, is encoded by the nucleic acid sequence of SEQ ID NO:11.

20 19. A method of treating a patient suffering from a pathophysiological condition that depends on angiogenesis, comprising:

providing to said patient an effective amount of a composition comprising a fusion protein comprising the A subunit

of Shiga-like bacterial toxin, or a truncated or mutated version thereof; and human vascular endothelial growth factor, or a truncated or mutated version thereof, said fusion protein possessing ribosome inactivating activity; and a

5 pharmaceutically acceptable carrier;

wherein said A subunit of said Shiga-like bacterial toxin, or a truncated or mutated version thereof, is encoded by the nucleic acid sequence of SEQ ID NO:9, and wherein said human vascular endothelial growth factor, or a truncated or mutated
10 version thereof, is encoded by the nucleic acid sequence of SEQ ID NO:11.

20. The method of claim 19, wherein said method is used in combination with other treatments for said pathophysiological
15 condition.

21. The method of claim 19, wherein the efficacy of said treatment is enhanced by decrease in oxygen or nutrient supplies that would arise from damage to endothelium caused by said
20 protein and pharmaceutical compositions.

22. An isolated nucleic acid comprising SEQ ID NO:9 and SEQ ID NO:11.

23. A fusion protein encoded by a nucleic acid sequence comprising SEQ ID NO:9 and SEQ ID NO:11.

24. An isolated nucleic acid comprising the nucleic acid
5 sequence of SEQ ID NO:11.

25. A fusion protein encoded by a nucleic acid having the nucleic acid sequence of SEQ ID NO:11.